

## **TÍTULO: ALZHEIMER'S DISEASE DIAGNOSTIC BIOMARKER, A METHOD AND KIT BASED ON THE SAME**

### **TECNOLOGY DESCRIPTION**

It is an in vitro diagnostic method for the diagnosis of EA based on new biomarkers.

It is an in vitro method for the diagnosis of Alzheimer's disease in which the glycosylation pattern of sAPP $\alpha$  and / or sAPP $\beta$  in a biological sample is determined, as well as a diagnostic kit for Alzheimer's disease, which comprises reagents to determine the glycosylation pattern of sAPP $\alpha$  and / or sAPP $\beta$  in a biological sample.

Therefore, this method comprises, on the one hand, the determination, in a biological sample of a subject, the glycosylation pattern of sAPP $\alpha$  and / or sAPP $\beta$  and, on the other, the comparison of said glycosylation pattern of sAPP $\alpha$  and / or sAPP $\beta$  with a reference sAPP $\alpha$  and / or sAPP $\beta$  glycosylation pattern, wherein a difference in said comparison is indicative of a positive diagnosis of Alzheimer's disease in said subject.

### **BUSINESS APLICATION SECTORS**

Sectors that develop research on neurodegenerative diseases, as well as pharmaceutical companies that develop diagnostic kits.

Likewise, University hospitals and research centers may be interested in the diagnostic kit.

### **TECNICAL ADVANTAGES AND BUSINESS BENEFITS**

One of the main advantages is that the original study analyzes APP directly in extracts of the cerebral cortex of EA and controls, at the expression level, protein level and glycosylation. Glycosylation is a co- and post-translational process specific to the cell type and moment of development, and pathology, which determines the interaction of proteins, their functionality and subsequent processing.

Through the proposed method, differences were found that indicated that altered APP glycosylation in the brain of subjects with EA mainly affects glycoforms processed by the non-amyloidogenic pathway.

### **TECNOLOGY DEVELOPMENT LEVEL**

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We are in a TRL6 phase, currently developing and validating a prototype kit to apply in a clinic laboratory.

### INTELLECTUAL PROPERTY RIGHTS

The patent is in co-ownership between the following entities:

- .- UMH =64%
- .- CIBERNED=30%
- .- CSIC =6%

### COLABORATION SEARCHED

We seek companies interested in carrying out prove of concept of the technology to facilitate the industrial application.

### RELATED IMAGES

Cerebro	Especie APP	%APP no ligado por la lectina			
		sAPP $\alpha$		sAPP $\beta$	
		Con A	PHA	Con A	PHA
Control	APP695	12.2 $\pm$ 1.7 [7.3-20.6]	6.6 $\pm$ 0.8 [4.3-9.4]	2.9 $\pm$ 0.8 [0.3-7.1]	2.6 $\pm$ 0.8 [0.2-6.8]
	APP-KPI	13.7 $\pm$ 2.1 [9.2-24.6]	5.7 $\pm$ 0.8 [2.8-8.1]	40.4 $\pm$ 4.6 [20.2-58.3]	37.0 $\pm$ 3.2 [22.6-51.0]
Alzheimer	APP695	7.0 $\pm$ 1.5 [2.4-12.9]	4.0 $\pm$ 0.6 [1.8-6.8]	1.2 $\pm$ 0.5 [0.1-3.7]	1.9 $\pm$ 0.3 [1.0-3.1]
	APP-KPI	7.7 $\pm$ 1.3 [4.0-12.4]	3.8 $\pm$ 0.6 [2.3-5.4]	57.1 $\pm$ 8.5 [37.6-89.0]	56.7 $\pm$ 9.7 [27.4-95.3]

Table: Percentage (%) of APP not bound by the lectins Con A (lectin from *Canavalia ensiformis* specific for mannoses) and PHA (subtype PHA-L, lectin from *Phaseolus vulgaris* specific for complex N-glycans with biantennial galactose-like structure with residues of N-acetylglucosamine) that specifically recognize different terminal sugars as indicated. The most abundant APP species in the brain (splicing variant APP695, neuronal, and glial variants APP751 / 770 called APP-KPI are separately determined for being carriers of the Kunitz-type serine protease inhibitor domain), and of them, by specific antibodies, the sAPP $\alpha$  and sAPP $\beta$  fragments. Differences between the same species and fragments, determined between control samples (n = 7 / group; frontal cortex extracts), non-pathological, and Alzheimer's are highlighted in red. In addition to those indicated, there are differences in the glycosylation of sAPP $\alpha$  and sAPP $\beta$ , indicating that glycosylation determines whether the processing of APP occurs via amyloidogenic or not.

### CONTACT DETAILS

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